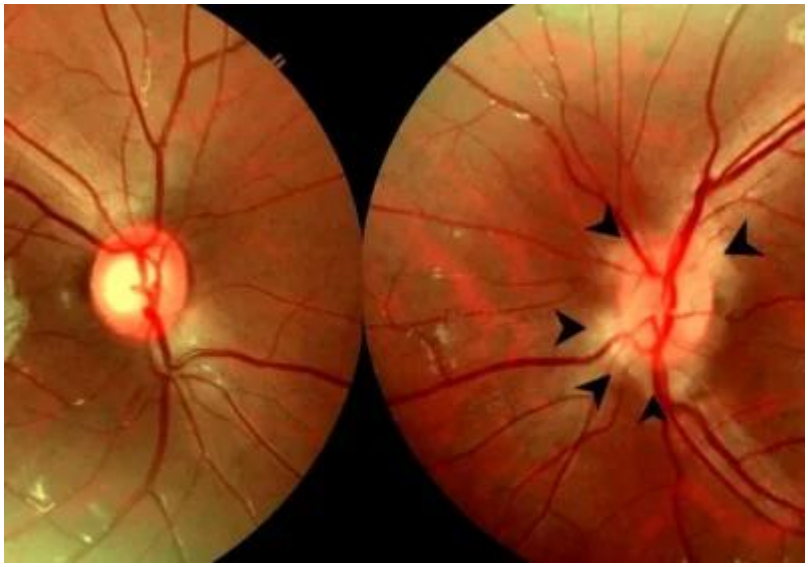
The neuromyelitis optica spectrum disorder (NMOSD) is a rare chronic, relapsing, demyelinating, autoantibody-mediated disease of the central nervous system (CNS). It is also called Devic disease. The classical manifestation of this disease encompasses transverse myelitis, optic neuritis (ON), brainstem syndrome, and area postrema syndrome, which manifests as episodes of intractable vomiting and hiccoughs. Approximately 75% of patients have antibodies against anti-aquaporin-4 (AQP4-Abs), a water channel expressed on astrocytes. In this study, the Chinese author investigated the presence of anti-myelin oligodendrocyte glycoprotein antibodies (MOG-Abs) and AQP4-Abs in COVID-19 vaccinated individuals, positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), who were diagnosed with new onset or relapse of optic neuritis.

Many pathogens, such as varicella-zoster, herpes simplex virus, *Mycoplasma*, and *Mycobacterium tuberculosis* can trigger a post-infectious immune-mediated ON and induce the anti-MOG and anti-AQP4 antibody production. Previous studies have described patients who were diagnosed with ON after COVID-19, suggesting that SARS-CoV-2 can trigger ON and the production of these antibodies.



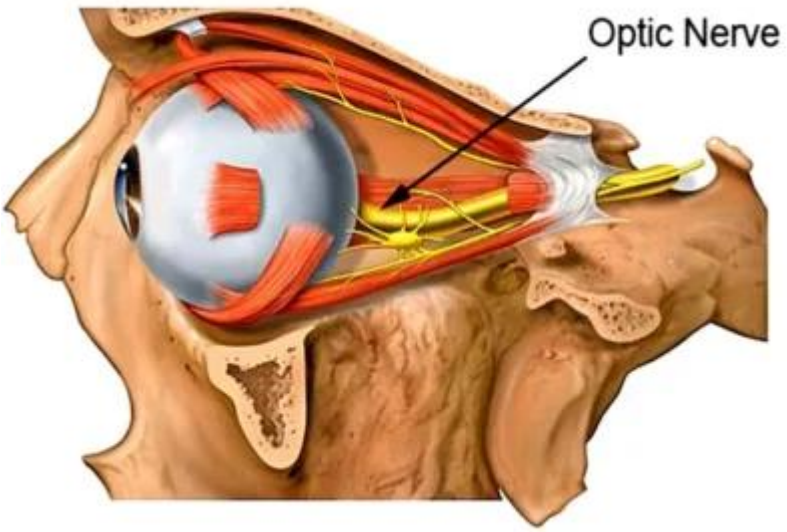
About the study

The author determined the seropositivity of anti-MOG-Abs and anti-AQP4-Abs in 35 patients with *de novo* onset or relapse of ON after COVID-19 using a cell-based indirect immunofluorescence assay. The presence of positive IgM or IgG antibodies against other pathogens, including *Treponema pallidum, Mycobacterium tuberculosis*, herpes viruses, hepatitis viruses, and human immunodeficiency virus (HIV), as well as other ocular diseases that may have an impact on the evaluation of ON were considered as the exclusion criteria.

SARS-CoV-2 infection was confirmed with positive reverse transcription polymerase chain reaction (rt-PCR) of nasopharyngeal swabs for SARS-CoV-2. All patients underwent a complete ophthalmic examination, color fundus photography, and visual field testing. 29 cases had an orbital or brain magnetic resonance imaging (MRI).

The serum samples were analyzed for anti-AQP4-Abs and anti-MOG-Abs. The sera were also tested for antibodies against other pathogens, such as *Treponema pallidum*, *Mycobacterium tuberculosis*, herpes viruses, hepatitis viruses, HIV, antinuclear antibodies, anti-double-stranded DNA, anti-Sjogren syndrome A or B antibodies, and anticardiolipin antibodies.

The mean follow-up period was 7.6 weeks, ranging from 8 to 16 weeks.



Results

The study included 35 individuals (46 eyes) with SARS-CoV-2 infection and confirmed diagnosis of optic neuritis. In 24 cases, ON occurred unilaterally, and in 11 cases bilaterally. The mean age of the patients was 38.2 years (6-69 years), and 17 of 35 were females.

All 35 patients with confirmed ON diagnosis received at least two doses of the inactivated COVID-19 vaccine (Sinovac). In 29 cases, the SARS-CoV-2 infection occurred on average 12.3 days before the onset of ON and vision loss. In only two cases, the systemic symptoms of viral infection occurred on average 11.5 days after the onset of ON and vision loss. Six patients had a previous medical history of ON. Three of them were positive for anti-AQP4-Abs and were treated with low-dose prednisone or immunosuppressive (azathioprine) therapy, whereas the remaining three cases had discontinued their medical treatment months or years before the relapse of ON and were negative for anti-AQP4-Abs and anti-MOG-Abs.

Ten of 35 patients with ON were positive for anti-MOG-Abs, while the remaining 21 patients with confirmed ON were negative for anti-MOG-Abs and anti-AQP4-Abs. An orbital or cranial MRI was performed in 29 of 35 patients and showed an optic nerve enlargement.

All 35 cases were seronegative for other pathogens. Three ON cases were positive for anti-β2-glycoprotein IgM antibodies, two for anticardiolipin IgM, two for antinuclear antibodies, one for anti-Ro-52 antibodies, and one for Sjogren’s syndrome antibodies.

Conclusion

This study has shown that SARS-CoV-2 infection can trigger the first onset or relapse of optic neuritis in COVID-19-vaccinated individuals. According to the author, molecular mimicry or exposure of the MOG protein to antigen-presenting cells during SARS-CoV-2-induced inflammation could be mechanisms responsible for the production of anti-MOG-Abs after SARS-CoV-2 infection. Since SARS-CoV-2 can compromise the blood-brain barrier, viral neuroinvasion (or its antigens) could lead to the release of central nervous system antigens such as AQP-4 into the systemic circulation, triggering the bystander immune response. Further studies are needed to clarify the link between SARS-CoV-2 infection and the production of ati-MOG-Abs.

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